

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference M0656/7046W0	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 99/ 19841	International filing date (day/month/year) 27/08/1999	(Earliest) Priority Date (day/month/year) 27/08/1998
Applicant MASSACHUSETTS INSTITUTE OF TECHNOLOGY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.
☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- ☒ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- 2
☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/19841

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 35-44 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the heparinase.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Claims 1-21,31,46-57,(all completely) 30,33-45 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-21,31,46-57 (all completely), 30,
33-45 (all partly)

A modified heparinase II, pharmaceutical preparation comprising it, method of cleaving a glycosaminoglycan with said heparinase II, nucleic acid encoding it, end vector and host cell comprising said nucleic acid.

2. Claims: 22-29, 32 (all completely), 30, 33-45 (all partly)

A modified heparinase I having enzymatic activity that is not dependent on the presence of calcium, pharmaceutical preparation comprising said heparinase I, method of cleaving a glycosaminoglycan employing said heparinase I

INTERNATIONAL SEARCH REPORT

In International Application No

PCT/US 99/19841

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/60 C12N9/88 A61K38/51 C12N11/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 34635 A (IBEX TECHNOLOGIES ;ZIMMERMANN JOSEPH (US)) 21 December 1995 (1995-12-21) page 32, line 1 - line 6; example 7 ---	1-21, 30, 31, 33, 34, 46-57
X	SHRIVER Z ET AL.: "Heparinase II from flavobacterium heparinum: Role of histidine residues in enzymatic activity as probed by chemical modification and site-directed mutagenesis" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 17, 24 April 1998 (1998-04-24), pages 10160-10167, XP002127285 MD US table I --- -/-	1-5, 7-13, 16, 17, 19-21, 30, 31, 33, 34, 46-52

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

27 January 2000

Date of mailing of the international search report

27.04.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

CUPIDO, M

INTERNATIONAL SEARCH REPORT

In International Application No

PCT/US 99/19841

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SASISEKHARAN R ET AL: "HEPARINASE I FROM FLAVOBACTERIUM HEPARINUM: THE ROLE OF THE CYSTEINE RESIDUE IN CATALYSIS AS PROBED BY CHEMICAL MODIFICATION AND SITE-DIRECTED MUTAGENESIS" BIOCHEMISTRY, US, AMERICAN CHEMICAL SOCIETY. EASTON, PA, vol. 34, no. 44, page 14441-14448 XP002026383 ISSN: 0006-2960 cited in the application the whole document ---	1-21
X,P	SHRIVER Z ET AL.: "Heparinase II from Flavobacterium heparinum: Role of cysteine in enzymatic activity as probed by chemical modification and site-directed mutagenesis" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 36, 4 September 1998 (1998-09-04), pages 22904-22912, XP002127286 MD US the whole document -----	1-21, 30, 31, 33, 34, 46-52

Information on patent family members

International Application No

PCT/US 99/19841

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9534635 A	21-12-1995	US 5681733 A	28-10-1997
		AU 694241 B	16-07-1998
		AU 2771095 A	05-01-1996
		CA 2192159 A	21-12-1995
		EP 0763101 A	19-03-1997
		JP 10511841 T	17-11-1998
		US 5919693 A	06-07-1999
		ZA 9504781 A	08-02-1996
